known to inhibit oxygen consumption in lymphosarcoma. He also carried out studies of the comparative permeability and respiration of normal and malignant cells afflicted with lymphatic leukemia. In some cases, though, Hogeboom's work on cancer became a tool for understanding features of normal metabolism. For example, tyrosine oxidase had been shown to catalyze the formation of melanin in plants and insects, but not in humans. In collaboration with Mark H. Adams, Hogeboom used cell fractionation techniques to isolate two enzymes from mouse melanoma cells. They first obtained a supernatant that catalyzed reactions of both tyrosine and dihydroxyphenylalanine (dopa). They then created two different precipitates with different saturations of ammonium sulfate, one of which catalyzed the tyrosine reaction while the other catalyzed the dopa reaction. In addition to identifying some of the characteristics of the two enzymes, they also observed that when centrifugation continued for several hours, most of the tyrosinase activity appeared in the sediment. They concluded, "This finding suggests that the enzyme may be associated with a particulate component of the cell (microsomes, Claude) and offers an explanation of its insolubility after precipitation by ammonium sulfate" (*Annual Report*, 1942–3, p. 85, see also Hogeboom & Adams, 1942).

In the same period Hogeboom was carrying out this work, Claude himself was becoming increasingly aware of the need to collaborate with biochemists in order to ascertain the enzyme constitution of his fractions. In the *Annual Report* for 1940–1, he noted, "Reports from other laboratories have demonstrated the association of these cell components with cytochrome oxidase, succinic acid dehydrogenase and phosphatase activity. Development of methods to extend the study of function is in progress" (p. 74). The following year he reported on a study with Dean Burk from Cornell which showed that both the large and small granule fractions were capable of taking up oxygen and concluded,

> This fact and the presence of relatively large amounts of iron and copper may indicate that these bodies are associated with the oxydoreduction activity of the cell. The larger granules isolated undoubtedly are what have been referred to as "secretory granules." Attempts are now being made to ascertain if special functional activities of various cells are centered in the granules. (Annual Report 1941–2, p. 74)

In 1942–3, Claude began to collaborate with Rollin Hotchkiss, a biochemist who had been in Dubos' laboratory until Dubos left for Harvard in July, 1942. Claude and Hotchkiss focused on d-amino acid oxidase, showing that it was